

Application No.: 09/889,085

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## REMARKS

### I. Applicants' Invention and Preliminary Comments.

Applicants thank the Examiner for the courtesy shown to co-inventor Ian Brown their representatives, Karen Kaiser and the undersigned attorney during the interview conducted July 13, 2005. The subject matter of the present invention as well as the disclosures of the applied references were discussed at the interview as well as cancellation of claims 41 and 76 which are hereby cancelled in favor of remaining claims 77-153 which recite the further limitation that the bacteria be "harvested."

As discussed at the Interview, Applicants' invention relates to the discovery that harvested bacteria which have been previously cultured in or grown on resistant starch and then subsequently incorporated into a product have improved viability and survival/recovery rates (compared with the same bacteria cultured in or grown on a medium not containing resistant starch). Thus, for example, Bifidobacteria grown on media containing resistant starch has a superior survival/recovery rate compared to the same strain of Bifidobacteria grown on media which does not contain resistant starch.

It is hypothesized that these improvements in the harvested bacteria are due to some biochemical change in the microbes themselves. However, as no conventional structural limitation to the microbes themselves can be added to the claims, the microbes can only be defined by the process steps by which they are made. Thus, Applicants have defined the microbes using process limitations which define how the novel microbes are produced. These process steps impart distinctive structural characteristics to the final microbes that manifest themselves in an improved survival/recovery rate. As was pointed out by Dr. Brown during the Interview, this improvement to the microbes is clearly evidenced by the examples presented in the specification.

### II. Outstanding Rejections

Claims 41, 76-77, 79, 81, 88, 90-105, 109-120, 124-135 and 139-150 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Masuda, U.S. Patent 5,143,845.

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Claims 41 and 76-153 remain rejected under 35 U.S.C. § 102(b) as being anticipated by Brown et al., U.S. Patent 6,060,050 in light of evidence by McNaught et al., U.S. Patent 5,714,600.

Claims 41 and 76-153 remain rejected under 35 U.S.C. § 103(a) as being unpatentable over Masuda taken with Brown et al. and McNaught et al.

Claims 41 and 76-153 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of Brown et al., U.S. Patent 6,221,350.

### III. Patentability Arguments

#### A. The Rejection of Claims 77, 79, 81, 88, 90-105, 109-120, 124-135 and 139-150 Under 35 U.S.C. §102(b) over Masuda et al. U.S. 5,143,845 Should be Withdrawn.

The rejection of claims 77, 79, 81, 90-105, 109-120, 124-135 and 139-150 under 35 U.S.C. § 102(b) as being anticipated by Masuda, et al. (US 5,143,845) should be withdrawn because Masuda fails to teach each element of the claims, particularly that the microbes have been grown or cultured in a media based on or containing resistant starch such that when subsequently harvested and incorporated in a product, the survival/recovery rate of the harvested microbes is increased.

The Examiner was unpersuaded by Applicants' previous arguments and Declaration which proved that there was no resistant starch in the microbial culture media of Masuda and that the claims are drawn to microbial preparations *per se*. The Examiner reminded Applicants that product-by-process claims are limited only by the final structure of the product obtained and that the patentability of a product does not depend upon its method of production. Applicants do not dispute these points but emphasize that their claims are drawn to the microbial preparations themselves and that those harvested microbes are different from those of the prior art.

Thus, the present invention pertains to microbes which are cultured on and harvested from resistant starch-based media. It has been discovered that such microbes are superior to those grown on other media in that they have improved survival/recovery rates. Thus, for example, Bifidobacteria grown on media containing resistant starch has a superior

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survival/recovery rate compared to the same strain of Bifidobacteria grown on media which does not contain resistant starch. It is hypothesized that this is due to some biochemical change in the microbes themselves. However, as no conventional structural limitation to the microbes themselves can be added to the claims, the microbes can only be defined by the process steps by which they are made. Thus, Applicants have defined the microbes using process limitations. These process steps impart distinctive structural characteristics to the final microbes, that of improved survival/recovery rate. This improvement to the microbes is clearly evidenced by the examples in the present application.

Product-by-process claims constitute a means by which Applicants can claim their inventions even where the nature of the invented product is such that it is difficult to define. Thus, the Supreme Court held in *Bonito Boats Inc. v. Thunder Craft Boats Inc.*, 489 U.S. 141, 9 USPQ 2d 1847, 1855 (1989) that "As long as the end product of the process is adequately defined as novel and nonobvious, a patent on the process may support a patent in the resulting product." Product-by-process claims are thus "perfectly acceptable [one] so long as the claims particularly point out and distinctly claim the product or genus of products for which protection is sought." *In re Brown and Saffer*, 173 USPQ 685, 688 (CCPA 1972). As stated in MPEP 2113, "the structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art." The MPEP continues by stating that this may be done by showing that the claimed product (microbe) exhibits unexpected properties compared with the prior art. This is supported by *In re Fessman*, 18 USPQ 324, 326 (CCPA 1974) in which the court states that it is "applicant's duty to present evidence which would demonstrate the unobvious character of his claimed invention over the cited reference."

Applicants have done exactly that; using the process steps to imply the structural difference of improved survival/recovery and then exemplifying the structural difference by comparing microbes cultured on resistant starch with those which were not.

Thus, the Application has provided evidence in the form of the various examples that microbes harvested from a resistant starch containing culture have improved survival and recovery compared to the same organisms harvested from media without resistant starch. (See each of Examples 1-11 and Figs. 1-14 corresponding thereto). Thus, it is clear that the products of the application are different from and represent an improvement over those of the

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prior art such as Masuda which are not grown in media containing resistant starch, and do not have this increased survival/recovery.

There is no evidence in Masuda which would indicate otherwise. The Examiner states that the microbes "effectively proliferate" and "demonstrate satisfactory effects upon administration." However, neither of these show that the microbes have improved survival/recovery. The Examiner also states that they are "characterized by heat stability, dry stability and drug stability". However, it is noted that this is "after spore formation" and it is well known in the art that spore formation provides increased stability of microorganisms and this differs from the present invention. Therefore, the present invention is novel over Masuda and the rejections of claims 77, 79, 81, 90-105, 109-120, 124-135 and 139-150 over Masuda should be withdrawn. Moreover, claims 102, 103, 117, 118, 120, 132, 133, 135, 147, 148 and 150 are further novel in that Masuda does not teach incorporating the microbes into the listed products.

**B. The Rejection of Claims 77-153 Under 35 U.S.C. §102(b) Over Brown et al. In View of McNaught et al. Should be Withdrawn.**

The rejection of claims 77-153 under 35 U.S.C. § 102(b) as being anticipated by Brown, et al. (US 6,060,050) in the light of evidence by McNaught, et al. (US 5,714,600) should be withdrawn because Brown '050 neither harvests microbes grown on resistant starch nor puts such microbes into products.

The Examiner was unpersuaded by Applicants' previous Response and argued that Brown "teaches microbial preparations grown on resistant starch", citing col. 5, lines 32-36 and figures 9 and 10. First, Brown neither harvests the microbes nor puts them into products. Brown grows fecal bacteria to count them. As one skilled in the art knows, harvesting microbes typically involves separating them from the media. This not only concentrates the microbes, but also typically removes by-products of the proliferation (e.g. fermentation). In contrast, counting or enumerating bacteria involves removing a small aliquot of bacteria with its environment (in the case of Brown, with fecal material) and allowing it to proliferate to count. For example, by spreading on agar, each microbe develops a colony such that one can count the bacteria in the original fecal sample.

Second, Brown neither provides any comparative experiment on a conventional substrate such as glucose nor identifies the improved survival/recovery of bacteria grown and

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harvested from resistant starch substrates. In contrast, the present invention shows improved survival/recovery rates of microbes grown on resistant starch. Further, as can be seen in the figures of Brown, the microbes have a lag time before they start to grow. In contrast, the presently claimed microbes do not display such lag time. For example, see figures 9A and 9B of the Brown reference and compare to Figure 1 of the present invention. This lag time is also shown in the present invention for microbes cultured on glucose in Figure 1. Thus, it is clear that the microbes cultured on resistant starch are different from those cultured on other media, such as glucose and the rejection has been overcome.

With respect to claims 78, 80, 82-87, 89-93, 106-108, 121-123, and 136-138, the claims further differ from the disclosure of Brown '050 in that there is no disclosure or suggestion in Brown that the microbes grown on resistant starch and harvested there from may be used in a microbial preparation containing resistant starch.

With respect to claims 94, 109, 124, and 139, the claims further differ from the disclosure of Brown '050 in that there is no disclosure or suggestion in Brown that the microbes are substantially resistant to stresses.

With respect to claims 100-108, 115-123, 131-138, and 146-150, the claims further differ in that there is no disclosure or suggestion in Brown that the microbes cultured on resistant starch may then be added to a product. Accordingly, the rejection of claims 77-153 over Brown '050 should be withdrawn.

**C. The Rejection Under 35 U.S.C. §103(a) over Masuda, Brown et al. and McNaught et al. Should be Withdrawn.**

Claims 77-153 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Masuda, et al. (US 5,143,845) taken with Brown I, et al. (US 6,060,050), Brown II, et al. (High amylose maize starch as a versatile prebiotic for use with probiotic bacteria, "Food Australia 50(12), December 1998, and McNaught, et al. (US 5,714,600).

As detailed above, Masuda does not disclose microbes which have been cultured on resistant starch. Accordingly, the Masuda microbes do not have superior recovery/survival compared to microbes not cultured on resistant starch. The Examiner acknowledges that Masuda lacks "disclosure about the use of resistant starch in the total product" but Brown I does not cure these deficiencies because it does not teach the use of resistant starch in the culture medium from which microbes are harvested as distinguished from being combined

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with microbes harvested from a different culture medium. Even if one skilled in the art was to combine the microbes of Masuda with resistant starch, they would not arrive at the present invention unless the resistant starch was used in the culture medium as well as being combined with the harvested microbes.

The Examiner applies Brown II for teaching that the addition of resistant starches into microbial products improves "robustness and viability of probiotics in the GI tract" and that high amylose resistant starch "enhances bacterial survival and stress resistance". As discussed at the Interview, this is not the Applicants' invention! The microbes of Brown II are ingested in combination with a resistant starch which physically protects the microbes. This is explained on page 608 which states that the "survival of the Bifidobacterium in the presence of the high amylose maize starch appears to be linked to the observation that some types of bacteria adhere to the surface of the starch granules" and that "these bacteria often demonstrated enhanced resistance to hostile conditions." This differs from the microbes of the present invention which have enhanced resistance whether or not resistant starch is present. This protection is the result of a change in the microbe itself from being cultured on resistant starch, and is not a physical protection.

While McNaught is relied upon by the Examiner to demonstrate that certain resistant starches are available in the prior art, it does not cure the remaining deficiencies mentioned above, particularly that microbes cultured on resistant starch and harvested there from have improved survival/recovery. For these reasons, the rejections of claims 77-153 should be withdrawn.

**D. The Rejection Under the Judicially Created Doctrine of Obvious-Type Double Patenting Over Brown et al. Should be Withdrawn.**

Finally, the obviousness-type double patenting rejection of claims 77-153 over claims 1-12 of U.S. Patent No. 6,221,350 ("Brown III") should also be withdrawn because the microbes of Brown III do not have the improved survival/recovery properties of the claimed microbes. This is because the Brown III microbes are cultured on media which do not contain resistant starch. While the microbes belong to the same species and are able to use resistant starch as a nutritional source they are not the same. Moreover, the capability of using resistant starch as a nutritional source and having been cultured on it clearly differ.

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Further, there is no disclosure in Brown III that the microbes are harvested. Thus, the rejection has been overcome.

The double patenting rejection also reflects a misunderstanding of the difference between the invention and of probiotic compositions. The probiotic compositions of Brown III comprise the combination of microbes and resistant starch but are not necessarily microbes which are the products of culturing on a resistant starch containing media (which resistant starch might have been consumed by the microbes and may no longer be present.) As discussed at the Interview, the improved microbial products of the present invention may optionally be used in place of conventional microbes to produce the probiotic compositions of Brown III but Brown III did not disclose the improved microbial products of the invention.

Accordingly, the obviousness type double patenting rejection should be withdrawn and each of claims 77-153 should be allowed.

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**CONCLUSION**

For all of the foregoing reasons, the Applicants respectfully request that the rejections should now be withdrawn and an early notice of all pending claims is respectfully solicited. Should the Examiner wish to discuss any issues of form or substance in order to expedite allowance of the pending application, she is invited to contact the undersigned attorney at the number indicated below.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 13-2855. If a fee is required for an extension of time under 37 C.F.R. §1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

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